

## COMMENTARY

# The ethics of paying for children's participation in research

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Paying for children's participation in research has become relatively common. A review of data from Center-Watch, a clinical trials listing service, suggests that nearly 25% of pediatric trials offer payment.<sup>1</sup> The amount of payment in the studies cited ranged from \$25 (to children) for a study of influenza medication to \$1500 (to families) for the time and travel involved in a study of medication for psoriasis.

Paying participants of any age remains controversial.<sup>2</sup> Some argue that payment may reduce participants' understanding or the voluntariness of their informed consent.<sup>3</sup> Others argue it may commodify research participation.<sup>4,7</sup> Conversely, *not* paying participants may be unethical: perhaps they should be rewarded for contributing to

the social good; perhaps they should share in the profits of research. Although these issues concern paying participants of any age, the current article focuses on the ethics of paying for *children*, persons under 18 years of age

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who by law cannot consent, to participate in research.

The literature offers minimal and, occasionally, conflicting guidance on paying for children's research participation. The US Federal regulations (45CFR46) offer no guidance, whereas the American Academy of Pediatrics (AAP) argues this practice is consistent with the "traditions and ethics of society," but advocates 2 safeguards. Parents should receive no more than "a token gesture of appreciation," and payments to children should not be disclosed until the study's end.<sup>5,6</sup> The Institutional Review Board (IRB) at Children's Memorial Hospital in Chicago prohibits direct cash payments and requires that payment for *healthy* children's participation go to the children.<sup>7</sup> More recently, the European Union has prohibited all "incentives or financial inducements" for pediatric research.<sup>8</sup>

To assess these recommendations and develop consistent guidelines, it will first be necessary to develop a general ethical analysis of paying for children's

research participation on the basis of 3 key questions: (1) when does payment raise ethical concerns? (2) which types of payment are most worrisome? and (3) what safeguards are needed to address these concerns?

Because children cannot consent, someone else, typically their parents, must decide whether to enroll them in research. Offers of payment raise ethical concerns then, because they have the potential to distort parents' decision-making; the opportunity for financial gain may lead parents to agree to research enrollment they otherwise would have opposed as contrary to their children's interests.

#### IRB Institutional Review Board

Some payments may *unwittingly* distort parents' decision-making. Research enrollment decisions are inherently complex, and the offer of payment may lead parents to unconsciously inflate the benefits and/or minimize the risks of their children's research participation. This possibility seems especially worrisome in the context of pediatric research because the primary decision makers, typically the child's parents, may benefit financially without having to face the risks. Payment may also entice some parents to *intentionally* take advantage of their role as primary decision-makers, ignoring risks and enrolling children for their own benefit.

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Finally, most children have limited experience with money, raising the possibility that payment may distort their decision-making as well. Because parents are the primary decision makers, distortions of children's decision making seem less worrisome. Nonetheless, this is a concern, particularly with respect to protocols that require children's "assent" or positive agreement.<sup>9</sup>

## TYPE OF PAYMENT FOR RESEARCH PARTICIPATION

To assess the ethical concerns raised by the potential for payment to distort parents' and children's decision making, it is critical to differentiate research-related payments into 4 different types:

1. **Reimbursement payments** compensate parents and children for their direct research-related expenses and should be based on the actual costs (eg, transportation, meals, lodging) that families incur.
2. **Compensation payments** compensate parents and children for the time and inconvenience of research participation. Levels of compensation payments should be a function of the demands (clinic visits, hospital stays, research procedures) that research places on families.
3. **Appreciation payments** are bonuses given after children's participation to thank them for their efforts.
4. **Incentive payments** encourage children's research enrollment. Payments may be designed to act as incentives, for instance, when an investigator intentionally reimburses families above their actual costs to encourage enrollment. Payments may also *inadvertently* act as incentives if they unintentionally exceed families' costs and,

thereby, act as incentives without being intended as such.

## DUE COMPENSATION

The potential for payment to distort parents' or children's decision making varies across the 4 types of payment. Reimbursement payments repay parents for the direct costs of research participation, ensuring that it is "revenue neutral." For this reason, reimbursement payments should not distort parents' or children's decision making and seem ethically acceptable. Indeed, it seems IRBs should consider requiring investigators to reimburse parents, particularly when they incur significant direct costs and the research offers little or no potential medical benefit.

Compensation payments are intended to "zero out" the incremental time, burdens, and inconveniences that research participation adds to families' lives, above direct financial outlays. Unfortunately, unlike reimbursement payments, the precise level of compensation needed to "zero out" families' research burdens cannot be determined simply by adding up their actual expenses. Instead, IRBs will have to estimate the point at which compensation payments "zero out" the level of burden that families have in a given protocol. The complexity of this determination introduces the possibility that compensation payments may sometimes inadvertently exceed families' actual burden, providing an incentive for them to enroll in research. The potential for compensation payments to act as inadvertent incentives is increased by the fact that a protocol's level of burden will vary from family to family, with protocols that seem burdensome to some families and innocuous to others.

In practice, investigators will not be able to determine the level of compensation needed to precisely "zero out" different families' burdens. Instead, research institutions should develop standardized levels of compensation for the

time children spend in research and the research procedures they undergo. It has been argued that compensation payments for the time *adults* spend in research should be commensurate with wages for unskilled, but essential, jobs.<sup>4</sup> Analogously, compensation payments for the time adolescents spend in research could be based on the minimum wage for teenagers, with children compensated for the time they are engaged in research activities.

To minimize the potential for compensation payments to distort parents' decision-making, they should be directed to the person who bears the burdens of research participation, typically the child. At the same time, some protocols require parents to contribute their own time, for instance, staying with a young child during research procedures. Banning all compensation payments to parents could block families with fewer economic resources from participating in such research. As with children's subjective sense of burden, the monetary value of a given amount of time will vary widely from family to family. To guard against the possibility that adequate compensation for some parents may act as an inadvertent incentive for others, compensation payments to parents should be calibrated to the economic resources of the least well-off families. By analogy to payment for adults who participate as *subjects*, payments to compensate parents who contribute to their children's research participation could be based on minimum wage levels for adults.

When calculated accurately, compensation payments ensure that children and their parents are compensated for the incremental time, burdens, and inconveniences that research participation adds to their lives. Hence, with these payments in place, additional appreciation payments seem unnecessary. In addition, if families learn before enrollment that appreciation payments are being offered, they may inadvertently act as incentives. This suggests the best approach may be to ban additional ap-

preciation payments, provided compensation levels are adequate.

By compensating families for the direct costs and burdens of research participation, reimbursement and compensation payments eliminate the financial obstacles that might keep most families from participating in research. It is hoped, with these obstacles eliminated, that families will decide to enroll in research because they want to help others and/or believe that the research is in the child's best interests. However, in some cases, even altruism and the potential for direct benefit to the child, combined with reimbursement and compensation payments, may not be enough to encourage sufficient enrollment. This possibility raises the central ethical concern related to pediatric payment: Is it ethical for investigators to offer incentive payments on top of appropriate reimbursement and compensation payments?

## BANS ON THE DISCLOSURE OF PAYMENTS

The American Academy of Pediatrics guidelines are meant to ensure that payment is not "part of the reason that a child volunteered or is volunteered for a study" by banning the *disclosure* of payments until the child's participation in research is completed.<sup>6</sup> Although this practice seems to eliminate payment's potential to distort parents' or children's decision to enroll in research, it raises a number of ethical concerns.

It is widely agreed that investigators should disclose the true nature of their research to subjects. Although a practice of nondisclosure does not involve outright deception, it does require investigators to conceal pertinent information and may lead families to the mistaken belief that payment is not being offered. A policy of nondisclosure would also place research teams in an awkward position when families ask

whether payment is being offered. Finally, even when research teams observe a strict policy of nondisclosure, families may learn through support networks or webpages that payment is being offered, raising the possibility that payments may act as inadvertent incentives.

## BANS ON INCENTIVE PAYMENTS

An alternative approach, advocated by the European Union, is to ban all payments that might act as incentives, eliminating the possibility that incentive payments might distort parents' or children's decision making. Given the importance of ensuring that families make research decisions consistent with children's interests, such bans seem defensible. But are they desirable?

Improving medical care for children is an important social goal, especially since so many treatments have not been validated for use in children. To the extent incentive payments are needed to recruit enough subjects to complete important research, banning them could hinder attempts to achieve this important social goal. This suggests that instead of banning incentive payments entirely, it makes sense to consider whether there are any alternatives that allow incentive payments, while minimizing their potential to distort parents' or children's decision making.

## MINIMIZING DISTORTED DECISION MAKING

Payment's potential influence on parents' decision making can be compared with its potential influence on physicians' decision making. Physicians' primary interest should be their patient's welfare; parents' primary interest should be their children's welfare. Just as offers of payment may distort physicians' consideration of patients' welfare, they may also distort parents' protec-

tion of their children's welfare. Borrowing from guidelines on physician's conflicts of interest suggests that addressing incentive payments' potential to distort decision making requires minimizing both the *likelihood* of distorted decision making, and the *magnitude* of its potential harms.

Policies that prohibit all incentives, such as the European Union's, seem to assume that payment should never be offered as a positive reason to enroll children in research because such offers, no matter how small, may distort parents' decision making. Although understandable, this view seems to overestimate the potential effect of relatively small incentives. For instance, relatively small incentive payments may be enough to convince parents to do things against which they have only a slight disinclination, such as driving their child to a research hospital, but not enough to get them to do things against which they have a stronger disinclination, such as enrolling their children in research that poses undue risks. Unfortunately, there are insufficient empirical data to determine precisely what levels of incentive payments might entice parents to enroll their children in research that is inconsistent with the children's interests. Until such data are developed, IRBs considering whether to approve incentive payments should carefully assess what levels would encourage children's research participation without distorting parents' decision making. In making these assessments, IRBs might appeal to existing community standards regarding appropriate incentives outside of the research context. For instance, what incentives are considered acceptable to encourage children to shovel snow from an infirm neighbor's sidewalk?

In some cases, IRBs may accept that incentives are needed to ensure sufficient enrollment, but remain concerned that the needed payments may distort parents' or children's decision-making. Presumably, the potential to distort families' decision-making will be negli-

gible when very small incentive payments, such as \$10, are offered. Moreover, the magnitude of any harms that result from families' distorted decision-making will be minor when the research poses little or no risks. However, concerns that payment may introduce an undue inducement should be carefully addressed when larger incentive payments are needed, and the research poses more than minor risks. In these cases, IRBs should consider requiring that a child advocate independently assess the appropriateness of the payment levels and families' decisions to enroll. In particular, the independent consultant could assess families' reasons for thinking that participation is consistent with the children's interests, for instance, by asking the children how they feel about the prospect of participating in the research and asking the parents what effect they think the research might have on their child.

Even when incentives do not distort families' decision-making, they may introduce a selection bias by increasing the number of families who enroll in research for the money. In addition, families who enroll in research for monetary gain may be less reliable research participants; they may be less likely to take medications on schedule, report side effects, attend required clinic visits, etc. To minimize payment's potential negative effect on pediatric research, IRBs should approve incentives in addition to reimbursement and compensation payments in limited cases only.

To consider an example, protocols without the potential for "important subject benefit" must obtain the assent of children who are capable of providing it (46.408). This requirement can make it difficult to complete certain minimal risk studies in younger children. For instance, many children 7 years to 11 years old have developed a sense of independence, but do not yet recognize the importance of research. These children may refuse to assent to a research survey or the provision of a saliva sample for biologic testing simply

because they would rather be playing with their friends. A \$5 incentive payment may be sufficient to encourage such children to give their assent (thus allowing researchers to complete important research) without being large enough to entice children's agreement to a study they recognize as contrary to their interests, such as one that includes procedures they find terrifying.

Finally, in addition to inappropriate inducements to *enroll* children in research, payments may provide an inappropriate inducement to *keep* children in research; parents and children may be unwilling to drop out for fear of losing money. To address this possibility, subjects who become ineligible after enrollment should receive any incentive payments that were offered but not yet delivered, and should receive pro-rated reimbursement and compensation for participation to date.

The *magnitude* of the harms that may result from distorted decision making depends on the extent to which children thereby are exposed to risks. Current Federal regulations allow children to be enrolled in research when the prospect of direct benefit "justifies" the risks. Children may be enrolled in research that does not offer a compensating potential for direct benefit only when the risks are no greater than a "minor increase" over the risks children face in everyday life (45CFR46.406).

By limiting the risks to which children may be exposed in research that does not offer a compensating potential for direct benefit, the Federal regulations may appear sufficient to address the potential harms of pediatric payment; as long as any "excess" risks are low, even payments that distort parents' decision making won't lead to serious harm. The problem with relying on the risk guidelines alone is that IRBs must make prospective risk assessments on the basis of the population of children they expect to be enrolled, not the specific children that actually do enroll. Even when IRBs make accurate risk assessments, the research may pose seri-

ous "idiosyncratic" risks to certain children. For instance, a brief magnetic resonance imaging scan that poses very low risks to the vast majority of children may pose serious risks to children with a morbid fear of loud noises. Given this possibility, it is important for parents to provide an additional confirmation that research enrollment poses acceptably low risks to their children in particular, yielding an important reason to ensure that payment does not distort their decision making. To this end, we consider 11 safeguards to minimize the likelihood that payment for pediatric research will distort parents' or children's decision making. The proposed additional safeguards are grouped by institutional guidelines, IRB review process, and mechanisms for payment.

### *Institutional Guidelines*

1. *Develop guidelines for all 4 types of payment.* Such guidelines should specify standards for reimbursement and compensation payments to avoid variation across similar protocols and minimize the extent to which compensation payments may act as inadvertent incentives. Institutions should consider requiring families to be reimbursed for anything more than minor direct costs. Compensation amounts for children should be determined on the basis of the accepted minimum wage payments for teenagers. Lower payments or nonmonetary forms of compensation are most appropriate for younger children. Guidelines should also consider banning appreciation payments, and allowing incentive payments in limited cases only, with strict limits on incentive amounts.
2. *Adopt an explicit policy on advertising payment for children's research participation.* These policies should specify the extent to which payment may be included in advertising for pediatric research. Mention of types of payment may be appro-

priate provided they are not emphasized and risks and burdens are also mentioned. Specific payment amounts should not be included in advertisements for pediatric research.

### ***The IRB Review Process***

3. *Require an explicit justification for all incentives.* Given the potential for distorted decision making, the default should be to limit payment to reimbursement and compensation. IRBs should approve payment beyond compensation levels only when it is within institutional limits and there is sufficient justification, for example, when data suggest payment is needed to recruit enough subjects.
4. *Allow children to be paid less than adults in identical studies.* Recent National Institutes of Health and Food and Drug Administration mandates to encourage children's participation in research may increase the number of children who participate in protocols designed for adults.<sup>10-12</sup> Because fairness recommends likes be treated alike, it may be assumed children should be paid the same as adults for equivalent burdens. However, even when adults and children assume the same level of burdens, they are not equal in other ways. Most importantly, a given amount of payment is likely to exert a greater influence on children's decision-making than adults' decision-making. When such influence could lead to distorted judgment, it seems appropriate, as expressed by most guidelines, to privilege protecting children over treating them like adults.
5. *Ensure payment to withdrawn subjects.* To minimize the chances that payment provides undue influence to keep children in research, subjects who become ineligible after enrolling should be ensured

reimbursement for expenses incurred, compensation for time and burdens to date, and any incentives that were offered but not yet delivered.

6. *Consider independent consent assessments in worrisome cases.* When compensation or incentive payments may represent an undue inducement to enroll in research that poses more than minor risks, the IRB should consider requiring an independent assessment by a child advocate. The advocate could assess the appropriateness of the level of payment and assess families' decision to enroll. Payment may be acceptable as a positive reason to enroll children in research, provided it does not entice parents or children to enroll in research that conflicts with the child's interests.
7. *Develop a general policy on describing payments in consent and assent forms.* Payments should be listed in a separate section of the consent and assent forms, not in the benefits section. Compensation payments should be described per unit of time or procedure, not as lump sums. How payment will be handled in the event of early withdrawal or disqualification should be described.

### ***Payment Mechanisms***

8. *Direct compensation payments to the proper party.* Payments to compensate for research participation should go to the person who bears the burden, typically the child.
9. *Avoid lump sum payments.* Large lump payments, such as \$2000, are more enticing than equivalent, pro-rated payments, such as \$40 per weekly clinic visit. To address this concern, reimbursement payments should be provided as costs are incurred, and compensation payments should be provided at regular intervals throughout research participation.

10. *Consider deferred payments.* Large sums, even when based on participation time and burdens, may distort parents' and children's decision making. Hence, for protocols that offer large sums, deferred payment mechanisms, such as savings bonds for the child, might be appropriate.

11. *Consider noncash payments.* Parents often exercise control over their children's assets. To minimize parents' access to children's payments, gift certificates redeemable at children's stores or the choice of an age-appropriate gift, such as a book, video, or movie pass, could be offered in lieu of money.

Ethical concerns over payment for children's research participation tend to regard all forms of payment as equally suspect. However, payments to reimburse for out-of-pocket expenses and to compensate for research time and burdens are ethically justifiable and should be strongly considered in cases where research-related costs are especially high and there is little or no potential for medical benefit. Although banning all incentive payments beyond reimbursement and compensation is ethically defensible, doing so runs the risk of impeding socially valuable pediatric research. To avoid this cost, small incentive payments may be acceptable when needed to ensure sufficient enrollment in important research.

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